General

Guideline Title

American Geriatrics Society 2015 updated Beers Criteria for potentially inappropriate medication use in older adults.

Bibliographic Source(s)

American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American Geriatrics Society 2015 updated Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2015 Nov;63(11):2227-46. [42 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: American Geriatrics Society 2012 Beers Criteria Update Expert Panel. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2012 Apr;60(4):616-31. [35 references]

This guideline meets NGC's 2013 (revised) inclusion criteria

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- May 10, 2016 – Olanzapine : The U.S. Food and Drug Administration (FDA) is warning that the antipsychotic medicine olanzapine can cause a rare but serious skin reaction that can progress to affect other parts of the body. FDA is adding a new warning to the drug labels for all olanzapine-containing products that describes this severe condition known as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS).
- May 3, 2016 – Aripiprazole (Abilify, Abilify Maintena, Aristada) : The U.S. Food and Drug Administration (FDA) is warning that compulsive or uncontrollable urges to gamble, binge eat, shop, and have sex have been reported with the use of the antipsychotic drug aripiprazole (Abilify, Abilify Maintena, Aristada, and generics). These uncontrollable urges were reported to have stopped when the medicine was discontinued or the dose was reduced. These impulse-control problems are rare, but they may result in harm to the patient and others if not recognized.
- March 22, 2016 – Opioid pain medicines : The U.S. Food and Drug Administration (FDA) is warning about several safety issues with the entire class of opioid pain medicines. These safety risks are potentially harmful interactions with numerous other medications, problems with the adrenal glands, and decreased sex hormone levels. They are requiring changes to the labels of all opioid drugs to warn about these risks.

Recommendations

Major Recommendations

Definitions of quality of evidence (high, moderate, low) and strength of recommendation (strong, weak, insufficient) are provided at the end of the "Major Recommendations" field.

Table. 2015 American Geriatrics Society (AGS) Beers Criteria for Potentially Inappropriate Medication Use in Older Adults

Organ System, Therapeutic Category, Drug	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
Anticholinergics				
First-generation Antihistamines • Brompheniramine • Carbinoxamine • Chlorpheniramine • Clemastine • Cyproheptadine • Dexbrompheniramine • Dexchlorpheniramine • Dimenhydrinate • Diphenhydramine (oral) • Doxylamine • Hydroxyzine • Meclizine • Promethazine • Triprolidine	Highly anticholinergic; clearance reduced with advanced age, and tolerance develops when used as hypnotic; risk of confusion, dry mouth, constipation, and other anticholinergic effects or toxicity Use of diphenhydramine in situations such as acute treatment of severe allergic reaction may be appropriate	Avoid	Moderate	Strong
Antiparkinsonian Agents • Benztropine (oral) • Trihexyphenidyl	Not recommended for prevention of extrapyramidal symptoms with antipsychotics; more-effective agents available for treatment of Parkinson disease	Avoid	Moderate	Strong
Antispasmodics • Atropine (excludes ophthalmic) • Belladonna alkaloids • Clidinium-chlordiazepoxide • Dicyclomine • Hyoscyamine • Propantheline • Scopolamine	Highly anticholinergic, uncertain effectiveness	Avoid	Moderate	Strong
Antithrombotics				
Dipyridamole, oral short-acting (does not apply to the extended-release	May cause orthostatic hypotension; more effective alternatives available; intravenous form acceptable for use in cardiac stress	Avoid	Moderate	Strong

The primary target audience is practicing clinicians. The intentions of the criteria are to improve the selection of prescription drugs by clinicians and patients; evaluate patterns of drug use within populations; educate clinicians and patients on proper drug usage; and evaluate health-outcome, quality-of-care, cost, and utilization data.

Organ System, Therapeutic Category, Drug	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
combination with aspirin)	testing			
Ticlopidine	Safer, effective alternatives available	Avoid	Moderate	Strong
Anti-infective				
Nitrofurantoin	Potential for pulmonary toxicity, hepatotoxicity, and peripheral neuropathy, especially with long-term use; safer alternatives available	Avoid in individuals with creatinine clearance <30 mL/min or for long-term suppression of bacteria	Low	Strong
Cardiovascular				
Peripheral Alpha-1 Blockers • Doxazosin • Prazosin • Terazosin	High risk of orthostatic hypotension; not recommended as routine treatment for hypertension; alternative agents have superior risk–benefit profile	Avoid use as an antihypertensive	Moderate	Strong
Central Alpha Blockers • Clonidine • Guanabenz • Guanfacine • Methyldopa • Reserpine (>0.1 mg/d)	High risk of adverse CNS effects; may cause bradycardia and orthostatic hypotension; not recommended as routine treatment for hypertension	Avoid clonidine as first-line antihypertensive. Avoid others as listed	Low	Strong
Disopyramide	Disopyramide is a potent negative inotrope and therefore may induce heart failure in older adults; strongly anticholinergic; other antiarrhythmic drugs preferred	Avoid	Low	Strong
Dronedarone	Worse outcomes have been reported in patients taking dronedarone who have permanent atrial fibrillation or severe or recently decompensated heart failure	Avoid in individuals with permanent atrial fibrillation or severe or recently decompensated heart failure	High	Strong
Digoxin	Use in atrial fibrillation: should not be used as a first-line agent in atrial fibrillation, because more-effective alternatives exist and it may be associated with increased mortality	Avoid as first-line therapy for atrial fibrillation	Atrial fibrillation: Moderate	Atrial fibrillation: Strong
	Use in heart failure: questionable effects on risk of hospitalization and may be associated with increased mortality in older adults with heart failure; in heart failure, higher dosages not associated with additional benefit and may increase risk of toxicity	Avoid as first-line therapy for heart failure	Heart failure: Low	Heart failure: Strong
	Decreased renal clearance of digoxin may lead to increased risk of toxic effects; further dose reduction may be necessary in patients with Stage 4 or 5 chronic kidney disease	If used for atrial fibrillation or heart failure, avoid dosages >0.125 mg/d	Dosage >0.125 mg/d: Moderate	Dosage >0.125 mg/d: Strong
Nifedipine, immediate release	Potential for hypotension; risk of precipitating myocardial ischemia	Avoid	High	Strong
Amiodarone	Amiodarone is effective for maintaining sinus rhythm in patients with atrial fibrillation, but it has numerous adverse effects	Avoid amiodarone as first-line therapy for prevention of atrial fibrillation	High	Strong

Organ System, Therapeutic Category, Drug	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
	rhythm but has greater toxicities than other antiarrhythmics used in atrial fibrillation; it may be reasonable first-line therapy in patients with concomitant heart failure or substantial left ventricular hypertrophy if rhythm control is preferred over rate control	line therapy for atrial fibrillation unless patient has heart failure or substantial left ventricular hypertrophy		
Central Nervous System				
Antidepressants, Alone or in Combination • Amitriptyline • Amoxapine • Clomipramine • Desipramine • Doxepin >6 mg/d • Imipramine • Nortriptyline • Paroxetine • Protriptyline • Trimipramine	Highly anticholinergic, sedating, and cause orthostatic hypotension; safety profile of low dose doxepin (6 mg/d) comparable with that of placebo	Avoid	High	Strong
Antipsychotics, First- (Conventional) and Second- (Atypical) Generation	Increased risk of cerebrovascular accident (stroke) and greater rate of cognitive decline and mortality in persons with dementia. Avoid antipsychotics for behavioral problems of dementia or delirium unless nonpharmacological options (e.g., behavioral interventions) have failed or are not possible *and* the older adult is threatening substantial harm to self or others	Avoid, except for schizophrenia, bipolar disorder, or short-term use as antiemetic during chemotherapy	Moderate	Strong
Barbiturates • Amobarbital • Butabarbital • Butalbital • Mephobarbital • Pentobarbital • Phenobarbital • Secobarbital	High rate of physical dependence, tolerance to sleep benefits, greater risk of overdose at low dosages	Avoid	High	Strong
Benzodiazepines Short- and intermediate-acting: • Alprazolam • Estazolam • Lorazepam • Oxazepam • Temazepam • Triazolam Long-acting: • Clorazepate	Older adults have increased sensitivity to benzodiazepines and decreased metabolism of long-acting agents; in general, all benzodiazepines increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle crashes in older adults May be appropriate for seizure disorders, rapid eye movement sleep disorders, benzodiazepine withdrawal, ethanol withdrawal, severe generalized anxiety disorder, and periprocedural anesthesia	Avoid	Moderate	Strong

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CNS = central nervous system; NSAIDs = nonsteroidal anti-inflammatory drugs.

Organ System, Therapeutic Category, Drug	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
• Chlordiazepoxide (alone or in combination with amitriptyline or clidinium) • Clonazepam • Diazepam • Flurazepam • Quazepam				
Meprobamate	High rate of physical dependence; very sedating	Avoid	Moderate	Strong
Nonbenzodiazepine, Benzodiazepine Receptor Agonist Hypnotics • Eszopiclone • Zolpidem • Zaleplon	Benzodiazepine receptor agonists have adverse events similar to those of benzodiazepines in older adults (e.g., delirium, falls, fractures); increased emergency department visits and hospitalizations; motor vehicle crashes; minimal improvement in sleep latency and duration	Avoid	Moderate	Strong
Ergoloid mesylates (dehydrogenated ergot alkaloids) Isoxsuprine	Lack of efficacy	Avoid	High	Strong
Endocrine				
Androgens • Methyltestosterone • Testosterone	Potential for cardiac problems; contraindicated in men with prostate cancer	Avoid unless indicated for confirmed hypogonadism with clinical symptoms	Moderate	Weak
Desiccated thyroid	Concerns about cardiac effects; safer alternatives available	Avoid	Low	Strong
Estrogens with or without progestins	Evidence of carcinogenic potential (breast and endometrium); lack of cardioprotective effect and cognitive protection in older women. Evidence indicates that vaginal estrogens for the treatment of vaginal dryness are safe and effective; women with a history of breast cancer who do not respond to nonhormonal therapies are advised to discuss the risk and benefits of low-dose vaginal estrogen (dosages of estradiol <25 µg twice weekly) with their healthcare provider	Avoid oral and topical patch Vaginal cream or tablets: acceptable to use low-dose intravaginal estrogen for management of dyspareunia, lower urinary tract infections, and other vaginal symptoms	Oral and patch: High Vaginal cream or tablets: Moderate	Oral and patch: Strong Topical vaginal cream or tablets: Weak
Growth hormone	Impact on body composition is small and associated with edema, arthralgia, carpal tunnel syndrome, gynecomastia, impaired fasting glucose	Avoid, except as hormone replacement after pituitary gland removal	High	Strong
Insulin, sliding scale	High risk of hypoglycemia without improvement in glycemic control	Avoid	Moderate	Strong

Organ System, Therapeutic Category, Drug	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
	regardless of care setting; refers to sole use of short- or rapid-acting insulins to manage or avoid hyperglycemia in absence of basal or long-acting insulin; does not apply to titration of basal insulin or use of additional short- or rapid-acting insulin in conjunction with scheduled insulin (i.e., correction insulin)			
Megestrol	Minimal effect on weight; increases risk of thrombotic events and possibly death in older adults	Avoid	Moderate	Strong
Sulfonylureas, Long-duration • Chlorpropamide • Glyburide	Chlorpropamide: prolonged half-life in older adults; can cause prolonged hypoglycemia; causes syndrome of inappropriate antidiuretic hormone secretion Glyburide: higher risk of severe prolonged hypoglycemia in older adults	Avoid	High	Strong
Gastrointestinal				
Metoclopramide	Can cause extrapyramidal effects, including tardive dyskinesia; risk may be greater in frail older adults	Avoid, unless for gastroparesis	Moderate	Strong
Mineral oil, given orally	Potential for aspiration and adverse effects; safer alternatives available	Avoid	Moderate	Strong
Proton-pump inhibitors	Risk of *Clostridium difficile* infection and bone loss and fractures	Avoid scheduled use for >8 weeks unless for high-risk patients (e.g., oral corticosteroids or chronic NSAID use), erosive esophagitis, Barrett's esophagitis, pathological hypersecretory condition, or demonstrated need for maintenance treatment (e.g., due to failure of drug discontinuation trial or H_2 blockers)	High	Strong
Pain Medications				
Meperidine	Not effective oral analgesic in dosages commonly used; may have higher risk of neurotoxicity, including delirium, than other opioids; safer alternatives available	Avoid, especially in individuals with chronic kidney disease	Moderate	Strong
Non-cyclooxygenase-selective NSAIDs, Oral • Aspirin >325 mg/d • Diclofenac • Diflunisal • Etodolac • Fenoprofen	Increases risk of gastrointestinal bleeding or peptic ulcer disease in high-risk groups, including those aged >75 or taking oral or parenteral corticosteroids, anticoagulants, or antiplatelet agents; use of proton-pump inhibitor or misoprostol reduces but does not eliminate risk. Upper gastrointestinal	Avoid chronic use, unless other alternatives are not effective and patient can take gastroprotective agent (proton pump inhibitor or misoprostol)	Moderate	Strong

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CNS = central nervous system; NSAIDs = nonsteroidal anti-inflammatory drugs.

Organ System, Therapeutic Category, Drug	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
• Ibuprofen • Ketoprofen • Meclofenamate • Mefenamic acid • Meloxicam • Nabumetone • Naproxen • Oxaprozin • Piroxicam • Sulindac • Tolmetin	ulcers, gross bleeding, or perforation caused by NSAIDs occur in approximately 1% of patients treated for 3–6 months and in ~2–4% of patients treated for 1 year; these trends continue with longer duration of use			
• Indomethacin • Ketorolac, includes parenteral	Indomethacin is more likely than other NSAIDs to have adverse CNS effects. Of all the NSAIDs, indomethacin has the most adverse effects. Ketorolac: Increased risk of gastrointestinal bleeding, peptic ulcer disease, and acute kidney injury in older adults	Avoid	Moderate	Strong
Pentazocine	Opioid analgesic that causes CNS adverse effects, including confusion and hallucinations, more commonly than other opioid analgesic drugs; is also a mixed agonist and antagonist; safer alternatives available	Avoid	Low	Strong
Skeletal Muscle Relaxants • Carisoprodol • Chlorzoxazone • Cyclobenzaprine • Metaxalone • Methocarbamol • Orphenadrine	Most muscle relaxants poorly tolerated by older adults because some have anticholinergic adverse effects, sedation, increased risk of fractures; effectiveness at dosages tolerated by older adults questionable	Avoid	Moderate	Strong
Genitourinary				
Desmopressin	High risk of hyponatremia; safer alternative treatments	Avoid for treatment of nocturia or nocturnal polyuria	Moderate	Strong
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Table. 2015 AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults Due to Drug-Disease or Drug-Syndrome Interactions That May Exacerbate the Disease or Syndrome

Disease or Syndrome	Drug(s)	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation

Disease or Syndrome	Drug(s)	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
Cardiovascular					
Heart failure	• NSAIDs and COX-2 inhibitors • Nondihydropyridine CCBs (diltiazem, verapamil)—avoid only for heart failure with reduced ejection fraction • Thiazolidinediones (pioglitazone, rosiglitazone) • Cilostazol • Dronedarone (severe or recently decompensated heart failure)	Potential to promote fluid retention and exacerbate heart failure	Avoid	NSAIDs: Moderate CCBs: Moderate Thiazolidinediones: High Cilostazol: Low Dronedarone: High	Strong

Syncope	• AChEIs
	• Peripheral alpha-1 blockers
	  • Doxazosin
	  • Prazosin
	  • Terazosin
	• Tertiary TCAs
	• Chlorpromazine
	• Thioridazine
	• Olanzapine
		Increases risk of orthostatic hypotension or bradycardia	Avoid	Peripheral alpha-1 blockers: High
				
				TCAs, AChEIs, antipsychotics: Moderate
					AChEIs, TCAs: Strong
					
					Peripheral alpha-1 blockers, antipsychotics: Weak

Central Nervous System					
Chronic seizures or epilepsy	• Bupropion • Chlorpromazine • Clozapine • Maprotiline • Olanzapine • Thioridazine • Thiothixene • Tramadol	Lowers seizure threshold; may be acceptable in individuals with well controlled seizures in whom alternative agents have not been effective	Avoid	Low	Strong

Delirium	• Anticholinergics (see Table 7 in the original guideline document for full list)
	• Antipsychotics
	• Benzodiazepines
	• Chlorpromazine
	• Corticosteroids[a]
	• H_2-receptor antagonists
	  • Cimetidine
	  • Famotidine
		Avoid in older adults with or at high risk of delirium because of the potential of inducing or worsening delirium
		
		Avoid antipsychotics for behavioral problems of dementia or delirium unless nonpharmacological options (e.g., behavioral
			Avoid	Moderate	Strong

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[a]Excludes inhaled and topical forms. Oral and parenteral corticosteroids may be required for conditions such as exacerbations of chronic obstructive pulmonary disease but should be prescribed in the lowest effective dose and for the shortest possible duration.

CCB = calcium channel blocker; AChEI = acetylcholinesterase inhibitor; CNS = central nervous system; COX = cyclooxygenase; NSAID = nonsteroidal anti-inflammatory drug; SSRIs = selective serotonin reuptake inhibitors; TCA = tricyclic antidepressant.

Disease or Syndrome	Drug(s)	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
	• Nizatidine • Ranitidine • Meperidine • Sedative hypnotics	interventions) have failed or are not possible *and* the older adult is threatening substantial harm to self or others Antipsychotics are associated with greater risk of cerebrovascular accident (stroke) and mortality in persons with dementia			

Dementia or cognitive impairment	• Anticholinergics (see Table 7 in original guideline document for full list)
	• Benzodiazepines
	• H_2-receptor antagonists
	• Nonbenzodiazepine, benzodiazepine receptor agonist hypnotics
	  • Eszopiclone
	  • Zolpidem
	  • Zaleplon
	• Antipsychotics, chronic and as-needed use
		Avoid because of adverse CNS effects
		
		Avoid antipsychotics for behavioral problems of dementia or delirium unless nonpharmacological options (e.g., behavioral interventions) have failed or are not possible *and* the older adult is threatening substantial harm to self or others. Antipsychotics are associated with greater risk of cerebrovascular accident (stroke) and mortality in persons with dementia
			Avoid	Moderate	Strong

History of falls or fractures	• Anticonvulsants
	• Antipsychotics
	• Benzodiazepines
	• Nonbenzodiazepine, benzodiazepine receptor agonist hypnotics
	  • Eszopiclone
	  • Zaleplon
	  • Zolpidem
	• TCAs
	• SSRIs
	• Opioids
		May cause ataxia, impaired psychomotor function, syncope, additional falls; shorter-acting benzodiazepines are not safer than long-acting ones
		
		If one of the drugs must be used, consider reducing use of other CNS-active medications that increase risk of falls and fractures (i.e., anticonvulsants, opioid-receptor agonists, antipsychotics, antidepressants, benzodiazepine receptor agonists, other sedatives and hypnotics) and implement other strategies to reduce fall risk
			Avoid unless safer alternatives are not available; avoid anticonvulsants except for seizure and mood disorders
			
			Opioids: avoid, excludes pain management due to recent fractures or joint replacement
				High
				
				Opioids: Moderate
					Strong
					
					Opioids: Strong

Insomnia	• Oral decongestants • Pseudoephedrine	CNS stimulant effects	Avoid	Moderate	Strong

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Disease or Syndrome	Drug(s)	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation

	• Phenylephrine
	• Stimulants
	  • Amphetamine
	  • Armodafinil
	  • Methylphenidate
	  • Modafinil
	• Theobromines
	  • Theophylline
	  • Caffeine				

Parkinson disease	• All antipsychotics (except aripiprazole, quetiapine, clozapine)
	• Antiemetics
	  • Metoclopramide
	  • Prochlorperazine
	  • Promethazine
		Dopamine-receptor antagonists with potential to worsen parkinsonian symptoms
		
		Quetiapine, aripiprazole, clozapine appear to be less likely to precipitate worsening of Parkinson disease
			Avoid	Moderate	Strong

Gastrointestinal					
History of gastric or duodenal ulcers	• Aspirin (>325 mg/day) • Non–COX-2 selective NSAIDs	May exacerbate existing ulcers or cause new or additional ulcers	Avoid unless other alternatives are not effective and patient can take gastroprotective agent (i.e., proton-pump inhibitor or misoprostol)	Moderate	Strong
Kidney and Urinary Tract					
Chronic kidney disease Stages IV or less (creatinine clearance <30 mL/min)	NSAIDs (non-COX and COX-selective, oral and parenteral)	May increase risk of acute kidney injury and further decline of renal function	Avoid	Moderate	Strong

Urinary incontinence (all types) in women	• Estrogen oral and transdermal (excludes intravaginal estrogen)
	• Peripheral alpha-1 blockers
	  • Doxazosin
	  • Prazosin
	  • Terazosin
		Aggravation of incontinence	Avoid in women	Estrogen: High
				
				Peripheral alpha-1 blockers: Moderate
					Estrogen: Strong
					
					Peripheral alpha-1 blockers: Strong

The primary target audience is the practicing clinician. The intentions of the criteria are to improve selection of prescription drugs by clinicians

Disease or Syndrome	Drug(s)	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
Lower urinary tract symptoms, benign prostatic hyperplasia	Strongly anticholinergic drugs, except antimuscarinics for urinary incontinence (see Table 7 in the original guideline document for complete list)	May decrease urinary flow and cause urinary retention	Avoid in men	Moderate	Strong

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[a]Excludes inhaled and topical forms. Oral and parenteral corticosteroids may be required for conditions such as exacerbations of chronic obstructive pulmonary disease but should be prescribed in the lowest effective dose and for the shortest possible duration.

CCB = calcium channel blocker; AChEI = acetylcholinesterase inhibitor; CNS = central nervous system; COX = cyclooxygenase; NSAID = nonsteroidal anti-inflammatory drug; SSRIs = selective serotonin reuptake inhibitors; TCA = tricyclic antidepressant.

Table. 2015 AGS Beers Criteria for Potentially Inappropriate Medications to Be Used with Caution in Older Adults

Drug(s)	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
Aspirin for primary prevention of cardiac events	Lack of evidence of benefit versus risk in individuals ≥80	Use with caution in adults ≥80	Low	Strong
Dabigatran	Increased risk of gastrointestinal bleeding compared with warfarin and reported rates with other target-specific oral anticoagulants in adults aged ≥75; lack of evidence of efficacy and safety in individuals with CrCl <30 mL/min	Use with caution in adults ≥75 or if CrCl <30 mL/min	Moderate	Strong
Prasugrel	Increased risk of bleeding in older adults; benefit in highest-risk older adults (e.g., those with prior myocardial infarction or diabetes mellitus) may offset risk	Use with caution in adults ≥75	Moderate	Weak
• Antipsychotics • Diuretics • Carbamazepine • Carboplatin • Cyclophosphamide • Cisplatin • Mirtazapine • Oxcarbazepine • SNRIs • SSRIs • TCAs • Vincristine	May exacerbate or cause syndrome of inappropriate antidiuretic hormone secretion or hyponatremia; monitor sodium level closely when starting or changing dosages in older adults	Use with caution	Moderate	Strong
Vasodilators	May exacerbate episodes of syncope in individuals with history of syncope	Use with caution	Moderate	Weak

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CrCl = creatinine clearance; SNRIs = serotonin-norepinephrine reuptake inhibitors; SSRIs = selective serotonin reuptake inhibitors; TCAs = tricyclic antidepressants.

Drug(s)	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation

Table. 2015 AGS Beers Criteria for Potentially Clinically Important Non-Anti-infective Drug–Drug Interactions That Should Be Avoided in Older Adults

Object Drug and Class	Interacting Drug and Class	Risk Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
ACEIs	Amiloride or triamterene	Increased risk of hyperkalemia	Avoid routine use; reserve for patients with demonstrated hypokalemia while taking an ACEI	Moderate	Strong
Anticholinergic	Anticholinergic	Increased risk of cognitive decline	Avoid, minimize number of anticholinergic drugs (see Table 7 in original guideline document)	Moderate	Strong
Antidepressants (i.e., TCAs and SSRIs)	≥2 other CNS-active drugs[a]	Increased risk of falls	Avoid total of ≥3 CNS-active drugs[a]; minimize number of CNS active drugs	Moderate	Strong
Antipsychotics	≥2 other CNS-active drugs[a]	Increased risk of falls	Avoid total of ≥3 CNS-active drugs[a]; minimize number of CNS active drugs	Moderate	Strong
Benzodiazepines and nonbenzodiazepine, benzodiazepine receptor agonist hypnotics	≥2 other CNS-active drugs[a]	Increased risk of falls and fractures	Avoid total of ≥3 CNS-active drugs[a]; minimize number of CNS active drugs	High	Strong
Corticosteroids, oral or parenteral	NSAIDs	Increased risk of peptic ulcer disease or gastrointestinal bleeding	Avoid; if not possible, provide gastrointestinal protection	Moderate	Strong
Lithium	ACEIs	Increased risk of lithium toxicity	Avoid, monitor lithium concentrations	Moderate	Strong
Lithium	Loop diuretics	Increased risk of lithium toxicity	Avoid, monitor lithium concentrations	Moderate	Strong
Opioid receptor agonist analgesics	≥2 other CNS-active drugs[a]	Increased risk of falls	Avoid total of ≥3 CNS-active drugs[a]; minimize number of CNS drugs	High	Strong
Peripheral alpha-1 blockers	Loop diuretics	Increased risk of urinary incontinence in older women	Avoid in older women, unless conditions warrant both drugs	Moderate	Strong
Theophylline	Cimetidine	Increased risk of theophylline toxicity	Avoid	Moderate	Strong
Warfarin	Amiodarone	Increased risk of bleeding	Avoid when possible; monitor international normalized ratio closely	Moderate	Strong
Warfarin	NSAIDs	Increased risk of bleeding	Avoid when possible; if used together, monitor for bleeding	High	Strong

[a]Central nervous system (CNS)-active drugs: antipsychotics, benzodiazepines, nonbenzodiazepine, benzodiazepine receptor agonist hypnotics; tricyclic antidepressants (TCAs); selective serotonin reuptake inhibitors (SSRIs); and opioids.

Object Drug and Class	Interacting Drug and Class	Risk Rationale	closely Recommendation	Quality of Evidence	Strength of Recommendation
[a]Central nervous system (CNS)-active drugs: antipsychotics; benzodiazepines; nonbenzodiazepine, benzodiazepine receptor agonist hypnotics; tricyclic antidepressants (TCAs); selective serotonin reuptake inhibitors (SSRIs); and opioids.					
ACEI = angiotensin-converting enzyme inhibitor; NSAID = nonsteroidal anti-inflammatory drug.					

Table. 2015 AGS Beers Criteria for Non-Anti-Infective Medications That Should Be Avoided or Have Their Dosage Reduced with Varying Levels of Kidney Function in Older Adults

Medical Class and Medication	Creatinine Clearance, mL/min, at Which Action Required	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
Cardiovascular or Hemostasis					
Amiloride	<30	Increased potassium, and decreased sodium	Avoid	Moderate	Strong
Apixaban	<25	Increased risk of bleeding	Avoid	Moderate	Strong
Dabigatran	<30	Increased risk of bleeding	Avoid	Moderate	Strong
Edoxaban	30-50 <30 or >95	Increased risk of bleeding	Reduce dose Avoid	Moderate	Strong
Enoxaparin	<30	Increased risk of bleeding	Avoid	Reduce dose	Strong
Fondaparinux	<30	Increased risk of bleeding	Avoid	Moderate	Strong
Rivaroxaban	30-50 <30	Increased risk of bleeding	Reduce dose Avoid	Moderate	Strong
Spironolactone	<30	Increased potassium	Avoid	Moderate	Strong
Triamterene	<30	Increased potassium, and decreased sodium	Avoid	Moderate	Strong
Central Nervous System and Analgesics					
Duloxetine	<30	Increased gastrointestinal adverse effects (nausea, diarrhea)	Avoid	Moderate	Weak
Gabapentin	<60	CNS adverse effects	Reduce dose	Moderate	Strong
Levetiracetam	≤80	CNS adverse effects	Reduce dose	Moderate	Strong
Pregabalin	<60	CNS adverse effects	Reduce dose	Moderate	Strong
Tramadol	<30	CNS adverse effects	Immediate release: reduce dose Extended release: avoid	Low	Weak
Gastrointestinal					
Cimetidine	<50	Mental status changes	Reduce dose	Moderate	Strong

Medical Class and Medication	Creatinine Clearance, mL/min, at Which Action Required	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
Famotidine	<50	Mental status changes	Reduce dose	Moderate	Strong
Nizatidine	<50	Mental status changes	Reduce dose	Moderate	Strong
Ranitidine	<50	Mental status changes	Reduce dose	Moderate	Strong
Hyperuricemia					
Colchicine	<30	Gastrointestinal, neuromuscular, bone marrow toxicity	Reduce dose; monitor for adverse effects	Moderate	Strong
Probenecid	<30	Loss of effectiveness	Avoid	Moderate	Strong
CNS = central nervous system					

Definitions

Quality of Evidence

High	Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes (≥2 consistent, higher-quality randomized controlled trials or multiple, consistent observational studies with no significant methodological flaws showing large effects)
Moderate	Evidence is sufficient to determine effects on health outcomes, but the number, quality, size, or consistency of included studies; generalizability to routine practice; or indirect nature of the evidence on health outcomes (≥1 higher-quality trial with >100 participants; ≥2 higher-quality trials with some inconsistency; ≥2 consistent, lower-quality trials; or multiple, consistent observational studies with no significant methodological flaws showing at least moderate effects) limits the strength of the evidence
Low	Evidence is insufficient to assess harms or risks in health outcomes because of limited number or power of studies, large and unexplained inconsistency between higher-quality studies, important flaws in study design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes

Strength of Recommendation

Strong	Benefits clearly outweigh harms, adverse events, and risks, or harms, adverse events, and risks clearly outweigh benefits
Weak	Benefits may not outweigh harms, adverse events, and risks
Insufficient	Evidence inadequate to determine net harms, adverse events, and risks

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Any disease or condition in older adults
- Adverse drug events
  - Drug-drug interactions
  - Drug-disease interactions
  - Inappropriate prescribing

Guideline Category

Evaluation

Management

Prevention

Risk Assessment

Clinical Specialty

Family Practice

Geriatrics

Internal Medicine

Pharmacology

Intended Users

Advanced Practice Nurses

Health Care Providers

Hospitals

Managed Care Organizations

Nurses

Patients

Pharmacists

Physician Assistants

Physicians

Public Health Departments

Guideline Objective(s)

To update the 2012 American Geriatric Society (AGS) Beers Criteria using a comprehensive, systematic review and grading of the evidence on drug-related problems and adverse drug events in older adults

Target Population

Populations aged 65 and older in all ambulatory and institutional settings of care in the United States, with the exception of hospice and palliative care

Interventions and Practices Considered

1. Avoidance of potentially inappropriate medications (PIMs)
2. Use of alternative medications

Major Outcomes Considered

- Prevalence of potentially inappropriate medication use in older adults
- Incidence of medication related problems and adverse drug events in geriatric population
- Mortality related to medication use

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Search

The literature from August 1, 2011 (the end of the previous panel's search) to July 1, 2014, was searched to identify published systematic reviews, meta-analyses, randomized controlled trials, and observational studies that were relevant to the project. The initial literature search was conducted on PubMed and the Cochrane Library. The drugs, drug classes, and conditions included in the 2012 criteria were used as initial search terms and were generally focused on "adverse drug events" and "adverse drug reactions." Individual drugs, drug classes, and conditions were searched individually and in combination. Search filters included human subjects, English language, and aged 65 and older. Case reports, case series, editorials, and letters were excluded. Clinical reviews were included for initial screening as potential background information and for reference list review. The initial searches identified 20,748 citations, of which 6,719 were selected for preliminary abstract review. The panel co-chairs reviewed 3,387 citations and abstracts, of which 2,199 were excluded for not meeting the study purpose or not containing primary data. At the time of the panel's face-to-face meeting, the co-chairs had selected 1,188 unduplicated citations for the full panel review. Subsequent searches (defined by panel workgroups) were conducted until December 15, 2014; some of these searches included studies published in the prior 10 years. The American Geriatric Society (AGS) also gave its members and members of the public a chance to submit evidence they felt the panel should consider. Any evidence submitted had to be evidence based and published in a peer-reviewed journal.

Number of Source Documents

Panel members reviewed abstracts, and evidence tables were developed for 342 studies, including 60 systematic reviews and meta-analyses, 49 randomized controlled trials, and 233 observational and other types of publications.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of Evidence

High	Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes (≥2 consistent, higher-quality randomized controlled trials or multiple, consistent observational studies with no significant methodological flaws showing large effects)
Moderate	Evidence is sufficient to determine effects on health outcomes, but the number, quality, size, or consistency of included studies; generalizability to routine practice; or indirect nature of the evidence on health outcomes (≥1 higher-quality trial with >100 participants; ≥2 higher-quality trials with some inconsistency; ≥2 consistent, lower-quality trials; or multiple, consistent

	observational studies with no significant methodological flaws showing at least moderate effects) limits the strength of the evidence
Low	Evidence is insufficient to assess harms or risks in health outcomes because of limited number or power of studies, large and unexplained inconsistency between higher-quality studies, important flaws in study design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

An independent researcher led the effort to prepare evidence tables and relied on the assistance of one other researcher for the initial drafts of evidence tables. The evidence tables included a summary of the study, as well as a quality rating and rating of the risk of bias for selected articles. The quality rating system was based on the Cochrane Risk of Bias and Jadad scoring system. The ratings were based on six critical elements: evidence of balanced allocation, allocation concealment, blinded outcome assessment, completeness of outcome data, selective outcome reporting, and other sources of bias. Following the Cochrane approach, each article was assigned a quality score (1–6 points) and a risk-of-bias rating. Low risk of bias was indicated by a low risk of bias in all six domains, unclear risk of bias was indicated by an unclear rating on one or more domains (others low) or a high risk of bias on one domain (others low or unclear), and high risk of bias was indicated by a high risk of bias on two or more domains. The independent researcher reviewed all evidence tables and proposed quality and risk-of-bias ratings before they were distributed to the expert panel to use for the Grades of Recommendation Assessment, Development and Evaluation (GRADE) rating process.

Methods Used to Formulate the Recommendations

Expert Consensus (Delphi)

Description of Methods Used to Formulate the Recommendations

Methods

For this new update, the American Geriatric Society (AGS) employed a well-tested framework that has long been used for development of clinical practice guidelines. Specifically, the framework involved the appointment of a 13-member interdisciplinary expert panel with relevant clinical expertise and experience and an understanding of how the criteria have been previously used. This framework also involved a development process using a modified Delphi method that included a systematic literature review and evaluation of the evidence base by the expert panel. Finally, the Institute of Medicine's 2011 report on developing practice guidelines, which included a period for public comments, guided the framework.

Panel Selection

A panel with expertise in geriatric medicine, nursing, pharmacy practice, research, and quality measures was convened comprising members of the previous panel and new members. Other factors that influenced selection of panel members were the desire to have interdisciplinary representation, a range of medical expertise, and representation from different practice settings (e.g., long-term care, ambulatory care, geriatric mental health, palliative care and hospice). In addition to the 13-member panel, representatives from the Centers for Medicare and Medicaid Services, National Committee for Quality Assurance, and Pharmacy Quality Alliance were invited to serve as ex-officio members.

Development Process

Since the previous update, the AGS had created a group to monitor the literature and to advise the 2015 expert panel of any articles relevant to the 2012 criteria and respond accordingly. Two members of the expert panel led this group, which was composed of members of the AGS Clinical Practice Committee and other expert members of AGS. The 2015 expert panel convened for a 2-day in-person meeting on July 28–29, 2014, to review the groups' findings and the results of the literature search. Panel discussions were used to define terms and to address questions of consistency, inclusion of infrequently used drugs, strategies for evaluating the evidence, consolidation or expansion of individual criterion, and development of renal dosage and drug–drug interaction tables. The panel then split into four groups, with each assigned a specific set of criteria for

evaluation. Groups were assigned as closely as possible according to specific area of clinical expertise (e.g., cardiovascular, central nervous system). Groups reviewed the literature search, selected citations relevant to their assigned criteria, and determined which citations they wanted to see the full-text article for and which should be abstracted into an evidence table. The groups then presented their findings to the full panel for comment and consensus. After the meeting, each group participated in a series of conference calls to continue the literature selection process and resolve any questions.

Each panelist independently rated the quality of evidence and strength of recommendation for each criterion using the American College of Physicians' Guideline Grading System (see the "Rating Scheme for the Strength of the Evidence" and the "Rating Scheme for the Strength of the Recommendations" field), which is based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) scheme developed previously. AGS staff compiled the panelist ratings for each group and returned them to that group, which then reached consensus in a conference call. Additional literature was obtained and included as needed. When group consensus could not be reached, the full panel reviewed the ratings and worked through any differences until consensus was reached. The panel judged each criterion as being a strong or weak recommendation on the basis of the quality of supporting evidence, the frequency and severity of harms, and the availability of better treatment alternatives. For some criteria, the panel provided a "strong" recommendation, even though the quality of evidence was low or moderate, when the potential for harm was substantial and safer or more-effective alternatives were available.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendation

Strong	Benefits clearly outweigh harms, adverse events, and risks, or harms, adverse events, and risks clearly outweigh benefits
Weak	Benefits may not outweigh harms, adverse events, and risks
Insufficient	Evidence inadequate to determine net harms, adverse events, and risks

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

After consensus was reached within the expert panel, the updated guidelines were circulated for peer review to relevant organizations and societies and posted to the American Geriatric Society (AGS) Web site for public comment. Organizations that participated in peer review are listed in the Acknowledgments section of the original guideline document. The panel reviewed and addressed all comments.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Careful application of the American Geriatrics Society (AGS) Beers Criteria by healthcare professionals, consumers, payors, and health systems should lead to closer monitoring of drug use. Dissemination of the criteria should lead to increased education and awareness of drug-related problems, increased reporting of drug-related problems, active patient and caregiver engagement and communication regarding medication use, targeted interventions to decrease adverse drug events in older adults, and improved outcomes.

Potential Harms

See the tables in the "Major Recommendations" field for descriptions of adverse drug events.

Contraindications

Contraindications

Androgens (methyltestosterone and testosterone) are contraindicated in men with prostate cancer.

Qualifying Statements

Qualifying Statements

- The goal of the 2015 American Geriatric Society (AGS) Beers Criteria continues to be improving the care of older adults by reducing their exposure to potentially inappropriate medications (PIMs). This is accomplished by using the criteria as an educational tool and quality measure—two uses that are not always in agreement. These criteria are not meant to be applied in a punitive manner. Prescribing decisions are not always clear-cut, and clinicians must consider multiple factors, including discontinuation of medications no longer indicated. Quality measures must be clearly defined, easily applied, and measured with limited information and thus, although useful, cannot perfectly distinguish appropriate from inappropriate care. The panel considered and vigorously discussed both roles during deliberations. The panel's review of evidence at times identified subgroups of individuals who should be exempt from a given criterion or to whom a specific criterion should apply. Such a criterion may not be easily applied as a quality measure, particularly when such subgroups cannot be easily identified through structured and readily accessible electronic health data. In these cases, the panel felt that a criterion should not be expanded to include all adults aged 65 and older when only certain subgroups have an adverse balance of benefits versus harms for the medication or conversely may be appropriate candidates for a medication that is otherwise problematic.
- Despite past and current efforts to translate the criteria into practice, some controversy and myths about their use in practice and policy continue to prevail. The panel addressed these concerns and myths by writing a companion piece to the updated criteria to address the best way for patients, providers, and health systems to use (and not use) the 2015 AGS Beers Criteria. Alternative suggestions to medications included in the current Use of High-Risk Medications in the Elderly and Potentially Harmful Drug-Disease Interactions in the Elderly quality measures are presented in another companion paper (see the "Availability of Companion Documents" field).
- The 2015 AGS Beers Criteria have several important limitations. Older adults are often underrepresented in drug trials. Thus, using an evidence-based approach may underestimate some drug-related problems or lead to weaker evidence grading. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) process was used for evidence grading, which allowed for rigor and greater transparency in the evidence grading process. The criteria cannot account for all individuals and special populations; for instance, they do not comprehensively address the needs of individuals receiving palliative and hospice care, in whom the balance of benefits and harms for many drugs on the list may differ from those of the general population of older adults. Finally, the search strategies used might have missed some studies published in languages other than English and studies available in unpublished technical reports, white papers, or other "gray literature" sources.
- The decisions and content of the 2015 AGS Beers Criteria are those of the AGS and the panel members and are not necessarily those of the U.S. government or U.S. Department of Veterans Affairs.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Mobile Device Resources

Patient Resources

Pocket Guide/Reference Cards

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Safety

Identifying Information and Availability

Bibliographic Source(s)

American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American Geriatrics Society 2015 updated Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2015 Nov;63(11):2227-46. [42 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2015 Nov

Guideline Developer(s)

American Geriatrics Society - Medical Specialty Society

Source(s) of Funding

American Geriatrics Society

Guideline Committee

American Geriatrics Society 2015 Beers Criteria Update Expert Panel

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

Each expert panel member completed a disclosure form at the beginning of the guideline process that was shared with the entire panel at the start of each panel meeting and call. Panel members who disclosed affiliations or financial interests with commercial entities are listed below. Panel members were asked to recuse themselves from discussions if they had a potential conflict of interest.

Dr. Beizer is an author and editor for LexiComp, Inc. Dr. Brandt is a consultant for Omnicare, Centers for Medicare and Medicaid Services, and University of Pittsburgh and a Section Editor for the *Journal of Gerontological Nursing* and received a grant from Econometrica. Dr. Fick is a paid consultant for SLACK Inc., is an editor for the *Journal of Gerontological Nursing*, and has current R01 funding from the National Institutes of Health and the National Institute of Nursing Research. Dr. Linnebur is a consultant for Colorado Access and Kindred Healthcare. Dr. Semla serves on the AARP Caregiver Advisory Panel, is an editor for LexiComp, and is a consultant for Omnicare. Dr. Semla's wife holds commercial interest in AbbVie (at which she is also an employee), Abbott, and Hospira. Dr. Semla receives honoraria from the AGS for his contribution as an author of Geriatrics at Your Fingertips and for serving as a section editor for the Journal of the American Geriatrics Society and is a past president and chair of the AGS Board of Directors. Dr. Steinman is a consult for Iodine.com, a web start-up company.

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: American Geriatrics Society 2012 Beers Criteria Update Expert Panel. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2012 Apr;60(4):616-31. [35 references]

This guideline meets NGC's 2013 (revised) inclusion criteria

Guideline Availability

Available from the Journal of the American Geriatrics Society Web site.

Availability of Companion Documents

The following are available:

- Steinman MA, Beizer JL, DuBeau CE, Laird RD, Lundebjerg NE, Mulhausen P. How to use the American Geriatrics Society 2015 Beers Criteria - a guide for patients, clinicians, health systems, and payors. J Am Geriatr Soc. 2015 Dec;63(12):e1-e7. Available from the Journal of the American Geriatrics Society Web site.
- Hanlon JT, Semla TP, Schmader KE. Alternative medications for medications in the use of high-risk medications in the elderly and potentially harmful drug-disease interactions in the elderly quality measures. J Am Geriatr Soc. 2015 Dec;63(12):e8-e18. Available from the Journal of the American Geriatrics Society Web site.
- AGS Beers Criteria for potentially inappropriate medication use in older adults. Pocket card. New York (NY): American Geriatrics Society; 2015. Available for purchase from the GeriatricsCareOnline.org Web site.

In addition, the 2015 Beers Criteria are available through the iGeriatrics mobile app, available for purchase from the GeriatricsCareOnline.org Web site.

Patient Resources

The following is available:

- Alternatives for medications listed in the AGS Beers Criteria for potentially inappropriate medication use in older adults. Patient handout. 2015 Oct. 3 p. Available to registered users from the GeriatricsCareOnline.org Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on August 23, 2012. The information was verified by the guideline developer on October 5, 2012. This summary was updated by ECRI Institute on May 22, 2014 following the U.S. Food and Drug Administration advisory on Eszopiclone (Lunesta). This summary was updated by ECRI Institute on April 3, 2015 following the U.S. Food and Drug Administration advisory on testosterone products. This summary was updated by ECRI Institute on September 18, 2015 following the U.S. Food and Drug Administration advisory on non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI Institute on February 15, 2016. The updated information was verified by the guideline developer on April 5, 2016. This summary was updated by ECRI Institute on May 24, 2016 following the U.S. Food and Drug Administration advisory on Olanzapine. This summary was updated by ECRI Institute on May 31, 2016 following the U.S. Food and Drug Administration advisory on Aripiprazole (Abilify, Abilify Maintena, Aristada). This summary was updated by ECRI Institute on June 2, 2016 following the U.S. Food and Drug Administration advisory on Opioid pain medicines.

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